General

Guideline Title

Menopause: diagnosis and management.

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Menopause: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Nov 12. 29 p. (NICE guideline; no. 23).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- October 25, 2016 – Testosterone and Other Anabolic Androgenic Steroids (AAS) : The U.S. Food and Drug Administration (FDA) approved class-wide labeling changes for all prescription testosterone products, adding a new Warning and updating the Abuse and Dependence section to include new safety information from published literature and case reports regarding the risks associated with abuse and dependence of testosterone and other AAS.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women's and Children's Health (NCC-WCH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Individualised Care

Adopt an individualised approach at all stages of diagnosis, investigation and management of menopause. Follow recommendations in the NICE

guideline on Patient experience in adult NHS services .

Diagnosis of Perimenopause and Menopause

Diagnose the following without laboratory tests in otherwise healthy women aged over 45 years with menopausal symptoms:

- Perimenopause based on vasomotor symptoms and irregular periods
- Menopause in women who have not had a period for at least 12 months and are not using hormonal contraception
- Menopause based on symptoms in women without a uterus

Take into account that it can be difficult to diagnose menopause in women who are taking hormonal treatments, for example for the treatment of heavy periods.

Do not use the following laboratory and imaging tests to diagnose perimenopause or menopause in women aged over 45 years:

- Anti-Müllerian hormone
- Inhibin A
- Inhibin B
- Oestradiol
- Antral follicle count
- Ovarian volume

Do not use a serum follicle-stimulating hormone (FSH) test to diagnose menopause in women using combined oestrogen and progestogen contraception or high-dose progestogen.

Consider using a FSH test to diagnose menopause only:

- In women aged 40 to 45 years with menopausal symptoms, including a change in their menstrual cycle
- In women aged under 40 years in whom menopause is suspected (see "Diagnosing and Managing Premature Ovarian Insufficiency" below)

Information and Advice

Give information to menopausal women and their family members or carers (as appropriate) that includes:

- An explanation of the stages of menopause
- Common symptoms (see recommendation below) and diagnosis
- Lifestyle changes and interventions that could help general health and wellbeing
- Benefits and risks of treatments for menopausal symptoms
- Long-term health implications of menopause

Explain to women that as well as a change in their menstrual cycle they may experience a variety of symptoms associated with menopause, including:

- Vasomotor symptoms (for example, hot flushes and sweats)
- Musculoskeletal symptoms (for example, joint and muscle pain)
- Effects on mood (for example, low mood)
- Urogenital symptoms (for example, vaginal dryness)
- Sexual difficulties (for example, low sexual desire)

Give information to menopausal women and their family members or carers (as appropriate) about the following types of treatment for menopausal symptoms:

- Hormonal, for example hormone replacement therapy (HRT)
- Non-hormonal, for example clonidine
- Non-pharmaceutical, for example cognitive behavioural therapy (CBT)

Give information on menopause in different ways to help encourage women to discuss their symptoms and needs.

Give information about contraception to women who are in the perimenopausal and postmenopausal phase. See guidance from the Faculty of Sexual & Reproductive Healthcare (FSRH) on Contraception for women aged over 40 years .

Offer women who are likely to go through menopause as a result of medical or surgical treatment (including women with cancer, at high risk of hormone-sensitive cancer or having gynaecological surgery) support and:

- Information about menopause and fertility before they have their treatment
- Referral to a healthcare professional with expertise in menopause

Managing Short-term Menopausal Symptoms

The recommendations in this section are not intended for women with premature ovarian insufficiency (see recommendations below for management of premature ovarian insufficiency).

Adapt a woman's treatment as needed, based on her changing symptoms.

Vasomotor Symptoms

Offer women HRT for vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks. Offer a choice of preparations as follows:

- Oestrogen and progestogen to women with a uterus
- Oestrogen alone to women without a uterus

Do not routinely offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone.

Explain to women that there is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms. However, explain that:

- Multiple preparations are available and their safety is uncertain
- Different preparations may vary
- Interactions with other medicines have been reported

Psychological Symptoms

Consider HRT to alleviate low mood that arises as a result of the menopause.

Consider CBT to alleviate low mood or anxiety that arise as a result of the menopause.

Ensure that menopausal women and healthcare professionals involved in their care understand that there is no clear evidence for SSRIs or SNRIs to ease low mood in menopausal women who have not been diagnosed with depression (see the NICE guideline on Depression in adults).

Altered Sexual Function

Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective. (At the time of publication [November 2015], testosterone did not have a UK marketing authorisation for this indication in women. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.)

Urogenital Atrophy

Offer vaginal oestrogen to women with urogenital atrophy (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms.

Consider vaginal oestrogen for women with urogenital atrophy in whom systemic HRT is contraindicated, after seeking advice from a healthcare professional with expertise in menopause.

If vaginal oestrogen does not relieve symptoms of urogenital atrophy, consider increasing the dose after seeking advice from a healthcare professional with expertise in menopause.

Explain to women with urogenital atrophy that:

- Symptoms often come back when treatment is stopped
- Adverse effects from vaginal oestrogen are very rare

- They should report unscheduled vaginal bleeding to their general practitioner (GP)

Advise women with vaginal dryness that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen.

Do not offer routine monitoring of endometrial thickness during treatment for urogenital atrophy.

Complementary Therapies and Unregulated Preparations

Explain to women that the efficacy and safety of unregulated compounded bioidentical hormones are unknown.

Explain to women who wish to try complementary therapies that the quality, purity and constituents of products may be unknown.

Advise women with a history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may be of benefit in the relief of vasomotor symptoms, there is uncertainty about:

- Appropriate doses
- Persistence of effect
- Variation in the nature and potency of preparations
- Potential serious interactions with other drugs (including tamoxifen, anticoagulants and anticonvulsants)

Review and Referral

Discuss with women the importance of keeping up to date with nationally recommended health screening.

Review each treatment for short-term menopausal symptoms:

- At 3 months to assess efficacy and tolerability
- Annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events)

Refer women to a healthcare professional with expertise in menopause if treatments do not improve their menopausal symptoms or they have ongoing troublesome side effects.

Consider referring women to a healthcare professional with expertise in menopause if:

- They have menopausal symptoms and contraindications to HRT or
- There is uncertainty about the most suitable treatment options for their menopausal symptoms

Starting and Stopping HRT

Explain to women with a uterus that unscheduled vaginal bleeding is a common side effect of HRT within the first 3 months of treatment but should be reported at the 3-month review appointment, or promptly if it occurs after the first 3 months (see recommendations on endometrial cancer in the NGC summary of the NICE guideline Suspected cancer: recognition and referral).

Offer women who are stopping HRT a choice of gradually reducing or immediately stopping treatment.

Explain to women that:

- Gradually reducing HRT may limit recurrence of symptoms in the short term
- Gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term

Women with, or at High Risk of, Breast Cancer

For advice on the treatment of menopausal symptoms in women with breast cancer or at high risk of breast cancer, see Section 1.3 of the NICE guideline Early and locally advanced breast cancer and the NGC summary of the NICE guideline Familial breast cancer: classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer.

Offer menopausal women with, or at high risk of, breast cancer:

- Information on all available treatment options
- Information that the SSRIs paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen
- referral to a healthcare professional with expertise in menopause

Long-term Benefits and Risks of Hormone Replacement Therapy

Venous Thromboembolism

Explain to women that:

- The risk of venous thromboembolism (VTE) is increased by oral HRT compared with baseline population risk
- The risk of VTE associated with HRT is greater for oral than transdermal preparations
- The risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline population risk

Consider transdermal rather than oral HRT for menopausal women who are at increased risk of VTE, including those with a body mass index (BMI) over 30 kg/m^2.

Consider referring menopausal women at high risk of VTE (for example, those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist for assessment before considering HRT.

Cardiovascular Disease

Ensure that menopausal women and healthcare professionals involved in their care understand that HRT:

- Does not increase cardiovascular disease risk when started in women aged under 60 years
- Does not affect the risk of dying from cardiovascular disease

Be aware that the presence of cardiovascular risk factors is not a contraindication to HRT as long as they are optimally managed.

Using Tables 1 and 2 in the original guideline document, explain to women that:

- The baseline risk of coronary heart disease and stroke for women around menopausal age varies from one woman to another according to the presence of cardiovascular risk factors
- HRT with oestrogen alone is associated with no, or reduced, risk of coronary heart disease
- HRT with oestrogen and progestogen is associated with little or no increase in the risk of coronary heart disease

Explain to women that taking oral (but not transdermal) oestrogen is associated with a small increase in the risk of stroke. Also explain that the baseline population risk of stroke in women aged under 60 years is very low (see Table 2 in the original guideline document).

Type 2 Diabetes

Explain to women that taking HRT (either orally or transdermally) is not associated with an increased risk of developing type 2 diabetes.

Ensure that women with type 2 diabetes and all healthcare professionals involved in their care are aware that HRT is not generally associated with an adverse effect on blood glucose control.

Consider HRT for menopausal symptoms in women with type 2 diabetes after taking comorbidities into account and seeking specialist advice if needed.

Breast Cancer

Using Table 3 in the original guideline document, explain to women around the age of natural menopause that:

- The baseline risk of breast cancer for women around menopausal age varies from one woman to another according to the presence of underlying risk factors
- HRT with oestrogen alone is associated with little or no change in the risk of breast cancer
- HRT with oestrogen and progestogen can be associated with an increase in the risk of breast cancer
- Any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT

Osteoporosis

Give women advice on bone health and discuss these issues at review appointments (see the NGC summary of the NICE guideline Osteoporosis: assessing the risk of fragility fracture).

Using Table 4 in the original guideline document, explain to women that the baseline population risk of fragility fracture for women around menopausal age in the UK is low and varies from one woman to another.

Using Table 4 in the original guideline document, explain to women that their risk of fragility fracture is decreased while taking HRT and that this benefit:

- Is maintained during treatment but decreases once treatment stops
- May continue for longer in women who take HRT for longer

Dementia

Explain to menopausal women that the likelihood of HRT affecting their risk of dementia is unknown.

Loss of Muscle Mass and Strength

Explain to women that:

- There is limited evidence suggesting that HRT may improve muscle mass and strength
- Muscle mass and strength is maintained through, and is important for, activities of daily living

Diagnosing and Managing Premature Ovarian Insufficiency

Diagnosing Premature Ovarian Insufficiency

Take into account the woman's clinical history (for example, previous medical or surgical treatment) and family history when diagnosing premature ovarian insufficiency.

Diagnose premature ovarian insufficiency in women aged under 40 years based on:

- Menopausal symptoms, including no or infrequent periods (taking into account whether the woman has a uterus) and
- Elevated FSH levels on 2 blood samples taken 4 to 6 weeks apart

Do not diagnose premature ovarian insufficiency on the basis of a single blood test.

Do not routinely use anti-Müllerian hormone testing to diagnose premature ovarian insufficiency.

If there is doubt about the diagnosis of premature ovarian insufficiency, refer the woman to a specialist with expertise in menopause or reproductive medicine.

Managing Premature Ovarian Insufficiency

Offer sex steroid replacement with a choice of HRT or a combined hormonal contraceptive to women with premature ovarian insufficiency, unless contraindicated (for example, in women with hormone-sensitive cancer).

Explain to women with premature ovarian insufficiency:

- The importance of starting hormonal treatment either with HRT or a combined hormonal contraceptive and continuing treatment until at least the age of natural menopause (unless contraindicated)
- That the baseline population risk of diseases such as breast cancer and cardiovascular disease increases with age and is very low in women aged under 40
- That HRT may have a beneficial effect on blood pressure when compared with a combined oral contraceptive
- That both HRT and combined oral contraceptives offer bone protection
- That HRT is not a contraceptive

Give women with premature ovarian insufficiency and contraindications to hormonal treatments advice, including on bone and cardiovascular health, and symptom management.

Consider referring women with premature ovarian insufficiency to healthcare professionals who have the relevant experience to help them manage all aspects of physical and psychosocial health related to their condition.

Clinical Algorithm(s)

An algorithm titled "Care algorithm" is provided in the original guideline document.

In addition, a National Institute for Health and Care Excellence (NICE) pathway titled "Menopause overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

Menopause

Guideline Category

Counseling

Diagnosis

Management

Treatment

Clinical Specialty

Family Practice

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

To provide advice for both healthcare professionals and women regarding menopause and the way symptom relief can be achieved

Target Population

- Menopausal women (covering the perimenopause and postmenopause)
- Women with premature ovarian insufficiency (irrespective of cause)

Note: This guideline does not cover:

- Women who are pregnant
- Women who are breastfeeding
- Men
- Transgender women

Interventions and Practices Considered

Assessment/Diagnosis

1. Symptom assessment
2. Serum follicle-stimulating hormone (FSH) test (as indicated)
3. Diagnosing premature ovarian insufficiency
    - Clinical history
    - Menopausal symptom assessment
    - Elevated FSH levels (2 blood samples taken 4 to 6 weeks apart)

Management/Treatment

1. Individualised care
2. Provision of information and advice to menopausal women and their family members or carers
3. Hormone replacement therapy (HRT) management of vasomotor symptoms
    - Oestrogen and progestogen to women with a uterus
    - Oestrogen alone to women without a uterus
    - Isoflavones and black cohosh
4. Management of psychological symptoms
    - HRT
    - Cognitive behavioural therapy (CBT)
5. Testosterone supplementation for management of altered sexual function
6. Management of urogenital atrophy
    - Vaginal oestrogen
    - Vaginal moisturisers and lubricants
7. Patient education regarding complementary therapies and unregulated preparations
8. Treatment review and referral to a healthcare professional with expertise in menopause
9. Starting and stopping HRT
10. Management of symptoms in women with, or at high risk of, breast cancer
11. Explanation of long-term benefits and risks of HRT
12. Managing premature ovarian insufficiency
    - Sex steroid replacement (HRT or a combined hormonal contraceptive)
    - Referral to healthcare professionals who have the relevant experience to help manage all aspects of related physical and psychosocial health

Note: The following were considered but not recommended: selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms; routine monitoring of endometrial thickness during treatment for urogenital atrophy.

Major Outcomes Considered

- Changes in menopausal symptom scores
- Reduction in frequency or intensity of vasomotor, musculoskeletal or psychological symptoms or alterations in sexual function
- Treatment-related adverse effects
- Health-related quality of life
- Mortality
- Coronary events
- Stroke or transient ischaemic attack
- Breast cancer
- Osteoporotic fractures
- Cognitive function and dementia
- Type 2 diabetes

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women and Children's Health (NCC-WCH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Protocols

Review questions were developed according to the type of question:

- Intervention reviews – in a PICO framework (patient, intervention, comparison and outcome)
- Reviews of diagnostic test accuracy – in a framework of population, index tests, reference standard and target condition
- Qualitative reviews – using population, area of interest and outcomes

These frameworks guided the literature searching process, critical appraisal and synthesis of evidence and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the NCC-WCH technical team and refined and validated by the group. The questions were based on the key clinical areas identified in the scope (see Appendix A in the full guideline appendices [see the "Availability of Companion Documents" field]).

A total of 17 review questions were identified (see Table 3 in the full version of the guideline).

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Clinical Literature Search

Systematic literature searches were undertaken to identify all published clinical evidence relevant to the review questions.

Databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to retrieve only articles published in English. All searches were conducted in MEDLINE, EMBASE and The Cochrane Library. All searches were updated on 22 January 2015. Due to the complexity of the network meta-analysis (NMA) and the time implications of updating the data analysis, searches were updated at an earlier date, on 13 January 2015. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews and asking the group members to highlight any additional studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix E in the full guideline appendices.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

During the scoping stage, a search was conducted for guidelines and reports on websites of organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. Searches for electronic, ahead-of-print publications were not routinely undertaken unless indicated by the Guideline Development Group (GDG). All references suggested by stakeholders at the scoping consultation were initially considered.

Reviewing and Synthesising the Evidence

The evidence was reviewed following these steps:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria in the review protocols (see Appendix D in the full guideline

appendices) and were presented in summary tables in each chapter and in evidence tables (see Appendix H in the full guideline appendices).

Health Economics

Refer to the "Cost Analysis" field and Appendix L in the full guideline appendices for information about the health economic literature search.

Number of Source Documents

Clinical Literature Search

Refer to Appendix F in the full guideline appendices (see the "Availability of Companion Documents" field) for flow diagrams of clinical selection, which detail the total number of studies included for each guideline topic.

Health Economics

A search of economic evidence relating to short term treatments for menopause symptoms identified 480 papers. After screening titles and abstracts 41 full text articles were retrieved for further review. Of these 41 studies, 9 were considered to be relevant to the review question and are summarised in Table 1 in Appendix L in the full guideline appendices.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

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Reviewing and Synthesising the Evidence

The evidence was reviewed following these steps:

- Full papers were reviewed against pre-specified inclusion and exclusion criteria in the review protocols (see Appendix D in the full guideline appendices [see the "Availability of Companion Documents" field]) and were presented in summary tables in each chapter and in evidence tables (see Appendix H in the full guideline appendices).

- Relevant studies were critically appraised using the appropriate checklist as specified in the NICE Guidelines Manual 2012 (see the "Availability of Companion Documents" field).
- Summaries of evidence were generated by outcome and were presented in Guideline Development Group (GDG) meetings:
    - Randomised studies – data were meta-analysed where appropriate and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles (for interventional reviews)
    - Observational studies – data were presented as a range of values or meta-analysed (where appropriate) in GRADE profiles and usually this was organised by outcomes
    - Diagnostic accuracy studies – presented as measures of diagnostic test accuracy (sensitivity, specificity, positive and negative likelihood ratio, area under the curve) in a modified version of a GRADE profile; a meta-analysis was not conducted when included studies were too heterogeneous
    - Qualitative studies – the themes of the studies were organised in summary evidence tables, along with quality assessment otherwise presented in a narrative form
- Of all data extracted, 80% was quality assured by a second reviewer and 50% of the GRADE quality assessment was quality assured by a second reviewer to minimise any potential risk of reviewer bias or error

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software or STATA. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes.

For the continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. A generic inverse variance option in RevMan5 was used if any studies reported solely the summary statistics and 95% confidence interval (95% CI) or standard error; this included any hazard ratios reported. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference was calculated from other reported statistics (probability [p] values or 95% CIs) if available: meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies that summarised results by presenting medians (and interquartile ranges), or only p values were given, this information was assessed in terms of the study's sample size and was included in the GRADE tables as a narrative summary. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for this evidence and this has been recorded in the footnotes of the GRADE tables.

In instances where multiple scales were reported for a single outcome, mean differences were standardised (divided by their standard deviation) before pooling, giving meta-analysed results that were reported as standardised mean differences (SMD), with a standard deviation of 1.

Where reported, time-to-event data were presented as a hazard ratio or results from a Cox hazard proportion model were given as a result from a multivariate analysis.

Stratified analyses were predefined for some review questions at the protocol stage when the group identified these strata to be different in terms of clinical characteristics and the interventions were expected to have a different effect, for example on the management of short-term symptoms. The reviewers stratified their analysis for women with a uterus, women without a uterus and women with a history of or at risk of breast cancer.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic (with an I-squared value of 50%–74.99% indicating serious inconsistency and I-squared value of over 75% indicating very serious inconsistency). If the heterogeneity still remained, a random effects model was employed to provide a more conservative estimate of the effect. Where considerable heterogeneity was present, the authors set out to perform predefined subgroup analyses based on the following factors:

- Different stages of menopause (peri- or postmenopausal)
- Different age groups

Data Synthesis for Diagnostic Test Accuracy Review

For diagnostic test accuracy studies, the following outcomes were reported:

- Sensitivity
- Specificity
- Positive and negative likelihood ratio

- Area under the curve (AUC)

Data Synthesis for Qualitative Review

For the qualitative review in the guideline, results were reported narratively either by individual study or by summarising the range of values as reported across similar studies. A summary evidence table was used when data allowed for this.

Data Synthesis Using Network Meta-analysis

A network meta-analysis (NMA) was formulated to synthesise direct and indirect evidence of treatments' efficacy to relieve short-term menopausal symptoms while preserving randomisation for the outcomes of frequency of vasomotor symptoms (VMS), discontinuation of treatment and vaginal bleeding. Hierarchical Bayesian NMAs with class effects were performed using the software WinBUGS version 1.4. Data from women in 3 distinct populations were used as inputs to the models: women with a uterus, women without a uterus and women with breast cancer or a history of breast cancer. The reviewers examined statistical models for fixed and random effects that allowed inclusion of multi-arm trials and accounted for the correlation between arms in the trials with any number of trial arms. These models were based on original work from the University of Bristol (https://www.bris.ac.uk/cobm/research/mpes/mtc.html).

As no dependency on time was identified, discontinuation of treatment and vaginal bleeding were treated as dichotomous outcomes and were modelled on the log-odds ratio scale. Frequency of VMS was distributed in the form of an overdispersed Poisson distribution and was therefore modelled on the log-mean ratio scale. On this scale, final and change from baseline frequencies of VMS could not be pooled, so a correlation coefficient was used to estimate final frequencies from change from baseline.

For all the networks set up in the NMA, models for fixed and random effects were developed and then these were compared based on residual deviance and deviance information criteria (DIC). The model with the smallest DIC is estimated to be the model that would best predict a replicate dataset which has the same structure as that currently observed. A small difference in DIC between the fixed and random effects models (3–5 points) implies that the better fit obtained by adding random effects does not justify the additional complexity. However, if the difference in DIC between a fixed and random effects model was less than 5 points, and the models make very similar inferences, then we would report the results from a fixed effects model as it does not make as many assumptions as the random effects model, contains fewer parameters and is easier for clinical interpretation than the random effects model.

Where closed loops of treatment comparisons existed in the networks, inconsistency was assessed by comparing any available direct and indirect treatment and testing the null hypothesis that the indirect evidence was no different from the direct evidence.

There were 3 main outputs from the NMA:

- The estimation of summary estimates (means ratios [MRs] or odds ratios [ORs]) (with their 95% credible intervals) were calculated for comparisons of the direct and indirect evidence
- The probability that each treatment was best based on the proportion of Markov chain iterations in which treatment had the highest probability of achieving the outcomes selected in the networks
- The ranking of treatments compared with baseline groups (presented as median rank and its 95% credible intervals)

The following sensitivity analyses were conducted:

- Changes to the value of the correlation coefficient used to estimate final frequencies of VMS from change from baseline
- Combining women with and without a uterus into a single population to determine if this led to changes in heterogeneity
- Removing low dose oral oestradiol plus progestogen to determine if this dose was reducing the overall efficacy of oral oestradiol plus progestogen in the model

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included randomised control trials (RCTs) and, where appropriate, observational studies was evaluated and presented using an adaptation of the GRADE toolbox developed by the international GRADE working group. The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. The clinical/economic evidence profile tables include details of the quality assessment and pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures of effect and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of randomised or completers) for binary outcomes. Reporting of publication bias was only taken into consideration in the quality assessment and included in the clinical evidence profile tables if it was apparent.

The selection of outcomes for each review question was decided when each review protocol was discussed with the GDG. However, given the nature of most of the review questions included in this guideline (driven by short- or long-term outcomes), the categorisation of outcomes as critical and important did not follow the standard GRADE approach. The outcomes selected for a review question were critical for decision-making in a specific context.

The evidence for each outcome in interventional reviews was examined separately for the quality elements listed and defined in Table 4 in the full version of the guideline. Each element was graded using the quality levels listed in Table 5 in the full version of the guideline.

The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious limitations. The ratings for each component were summed to obtain an overall assessment for each outcome (see Table 6 in the full version of the guideline).

The GRADE toolbox is designed only for RCTs and observational studies but the reviewers adapted the quality assessment elements and outcome presentation for diagnostic accuracy and qualitative studies, subject to data availability. For example, for diagnostic accuracy studies, the GRADE tables were modified to include the most appropriate measures of diagnostic accuracy (sensitivity, specificity, positive and negative likelihood ratio) whereas qualitative studies were presented in summary evidence tables around themes identified or direct participants' quotations. Quality of the evidence in the qualitative reviews was assessed per study level.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using the GRADE approach:

- A quality rating was assigned based on the study design. RCTs start as high, observational studies as moderate and uncontrolled case series as low or very low.
- The rating was then downgraded for the specified criteria: risk of bias (study limitations); inconsistency; indirectness; imprecision; and publication bias. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was a large magnitude of effect or a dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
- The downgraded/upgraded ratings were then summed and the overall quality rating was revised. For example, all RCTs started as high and the overall quality became moderate, low or very low if 1, 2 or 3 points were deducted respectively.
- The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in Sections 3.3.3.2 to 3.3.3.6 in the full version of the guideline.

Quality Assessment of NMA

For the NMAs, quality was assessed by looking at risk of bias across the included evidence (using the standard GRADE approach for this domain), heterogeneity and inconsistency.

The following limits of the upper 95% CI for between-study standard deviation were used to assess heterogeneity:

- Less than 0.3 – low heterogeneity; quality of evidence not downgraded
- 0.3 to 0.6 – moderate heterogeneity; quality of evidence downgraded by 1 level
- 0.6 to 0.9 – high heterogeneity; quality of evidence downgraded by 2 levels
- 0.9 to 1.2 – very high heterogeneity; quality of evidence downgraded by 3 levels

Inconsistency in NMA has a different meaning than in pairwise meta-analysis, referring to the discrepancy between direct and indirect evidence in closed treatment loops within the network. If closed treatment loops existed then the following criteria were adopted:

- Significant inconsistency in 1 loop – quality of evidence downgraded by 1 level
- Significant inconsistency in more than 50% of loops where several loops exist – quality of evidence downgraded by 2 levels

For fixed-effect NMAs that did not model heterogeneity, or for networks in which inconsistency could not be assessed as no closed treatment loops existed, these criteria were not considered to impact the quality of evidence.

Quality Assessment of Qualitative Studies

Quality of qualitative studies (at study level) was assessed following the NICE checklists in The Guidelines Manual 2007 (see the "Availability of Companion Documents" field). The main quality assessment domains are organised across the definition of population included, the appropriateness of methods used and the completeness of data analysis and the overall relevance of the study participants to the population of interest for the guideline.

Use of Absolute Effect in Decision-making

The GDG assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio with the exception of estimation of baseline risk for breast cancer and cardiovascular disease (CVD) (see Section 3.3.4 in the full version of the original guideline document for details).

Evidence Statements

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by comparison (for interventional reviews) or by description of outcome where appropriate and encompass the following key features of the evidence:

- The number of studies and the number of participants for a particular outcome
- A brief description of the participants
- An indication of the direction of effect (if 1 treatment is beneficial or harmful compared with the other, or whether there is no difference between the 2 tested treatments)
- A description of the overall quality of evidence (GRADE overall quality)

Health Economics

Refer to the "Cost Analysis" field and Appendix L in the full guideline appendices for information about the health economic literature search.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women and Children's Health (NCC-WCH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Who Developed This Guideline?

A multidisciplinary Guideline Development Group (GDG) comprising healthcare professionals and researchers as well as lay members developed this guideline (see the list of group members and acknowledgements). NICE funds the NCC-WCH and thus supported the development of this guideline. The GDG was convened by the NCC-WCH and chaired by Professor Mary Ann Lumsden in accordance with guidance from NICE.

The group met every 4 to 6 weeks during the development of the guideline. At the start of the guideline development process all group members declared interests including consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. At all subsequent group meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix C in the full guideline appendices (see the "Availability of Companion Documents" field).

Staff from the NCC-WCH provided methodological support and guidance for the development process. The team working on the guideline included a guideline lead, a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the

guideline in collaboration with the group.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature: all evidence tables are in Appendix H in the full guideline appendices
- Summary of clinical and economic evidence and quality assessment (as presented in Chapters 4 to 11 in the full version of the guideline)
- Forest plots (Appendix J in the full guideline appendices)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix L in the full guideline appendices)

Recommendations were drafted on the basis of the group's interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally, in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes, although most of the reviews in the guideline were outcome driven. When this was done informally, the group took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the group's values and preferences), and the confidence the group had in the evidence (evidence quality). Secondly, the group assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the group drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The group also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

The wording of recommendations was agreed by the group and focused on the following factors:

- The actions healthcare professionals need to take
- The information readers need to know
- The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations)
- The involvement of patients (and their carers if needed) in decisions about treatment and care
- Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective intervention

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter of the original guideline document.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The aims of the health economic input to the guideline were to inform the Guideline Development Group (GDG) of potential economic issues related to diagnosis and management of menopause to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years [QALYs]), harms and costs of different care options.

The group prioritised a single review question – on managing the short-term symptoms of menopause – where it was thought that economic considerations would be particularly important in formulating recommendations and a review of the health economic literature was also undertaken for this question. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using the economic evaluations checklist as specified in the National Institute for Health and Care Excellence (NICE) guidelines manual (see the "Availability of Companion Documents" field).

Health economic reviews were undertaken for review questions relating to short-term treatment and symptoms, the diagnosis of premature ovarian insufficiency (POI) and the treatment of urogenital atrophy in women with menopause-related vaginal/urogenital atrophy.

No health economic literature review was reported for the long-term risks and benefits of hormone replacement therapy (HRT). It was agreed that the economic analysis would not address the impact of HRT beyond 5 years because authors of studies considering a longer term impact have reported that cost effectiveness is driven by differences in short-term symptom relief. In the context of this guideline it was not considered appropriate to investigate the cost effectiveness of a treatment that looked only at a health economic evaluation of long-term symptoms without considering the impact on short-term symptoms. Therefore relevant studies considering longer term risks and benefits would have been expected to have been captured by the systematic review the reviewers had planned on short-term treatments. However, the absence of a health economic review did not preclude the use of data from the clinical review of longer term risks and benefits in the health economic analysis if the group considered that there were important longer term risks and benefits from short-term use of HRT.

No health economic review was undertaken on the review question focused on information and advice as this focused primarily on the content and quality of information that is routinely provided rather than whether the provision of information itself represent a cost-effective use of resources. Therefore, this question was not primarily about competing alternatives which have different opportunity costs and therefore was not considered suitable for a health economic review.

No clinical evidence was identified for classification systems for the diagnosis of menopause and it was thought a priori that it was most unlikely that there would be economic studies on this. Similarly, no clinical evidence was found on the intervals at which clinical review be undertaken to assess the effectiveness and safety of treatments to relieve menopausal symptoms and to determine when women need to be referred to specialist care and again it was thought *a priori* that it would be very unlikely that any economic evaluation would exist on this topic.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Validation Process

This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) Web site when the pre-publication check of the full guideline occurs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

Type of Studies

Randomised controlled trials (RCTs), non-randomised trials and observational studies (including diagnostic or comparative cohorts) were included in the evidence reviews as appropriate.

Literature reviews, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

For most intervention reviews in this guideline, parallel RCTs were included because they are considered the most robust study design for unbiased estimation of intervention effects. Crossover RCTs were appropriate for some of the interventional questions.

If there was limited evidence from RCTs, well-conducted non-randomised comparative studies were included. For most review questions investigating long term outcomes of hormone replacement therapy (HRT), prospective comparative studies with adjusted analyses on important confounders were selected in addition to RCTs. Please refer to Appendix D in the full guideline appendices (see the "Availability of Companion Documents" field) for full details on the study design of studies selected for each review question.

For diagnostic reviews, cross-sectional and retrospective studies were included. Case-control or case series were not included for the presentation of evidence for any review question.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Optimal clinical management of menopause-related symptoms, including hormonal and non-hormonal therapies to improve quality of life

Refer to the "Consideration of clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for benefits of specific interventions.

Potential Harms

- Unscheduled vaginal bleeding is a common side effect with combined hormone therapy, but if persistent beyond 3 months then investigation may be required depending on the degree of clinical concern.
- The Women's Health Initiative initially reported that although hormone replacement therapy (HRT) prevented osteoporotic fractures and colon cancer, it increased the risk of having a cardiovascular event as well as the incidence of breast cancer. However, the association between HRT and cardiovascular disease (CVD) has since been disputed and the data are now being reinterpreted.
- An increase in the risk of venous thromboembolism (VTE) (deep vein thrombosis [DVT] or pulmonary embolism [PE]) is a significant side effect of HRT particularly because PEs can be fatal. This risk appears to be greater with oral than transdermal HRT. DVT risk increases with age and body mass index (BMI), among other risk factors.

Refer to the "Consideration of clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for harms of specific interventions.

Contraindications

Contraindications

Hormone replacement therapy (HRT) is contraindicated in women who have (or are at high risk of) hormone-dependent cancer.

Qualifying Statements

Qualifying Statements

- Healthcare professionals are expected to take the National Institute for Health and Care Excellence (NICE) clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
- The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.
- Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.
- The National Collaborating Centre for Women and Children's Health (NCC-WCH) disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

Implementation of the Guideline

Description of Implementation Strategy

Menopause Implementation: Getting Started

This section highlights 3 areas of the menopause guideline that could have a big impact on practice and be challenging to implement, along with the reasons why the authors are proposing change in these areas. The section also gives information on resources to help with implementation.

The Challenge: Stopping the Use of Follicle-stimulating Hormone Tests to Diagnose Menopause in Women Aged Over 45 Years

The follicle-stimulating hormone (FSH) test is often performed unnecessarily in women aged over 45 years. The evidence underpinning this guideline highlights that hormonal tests should not routinely be used in the diagnosis of menopause and that FSH tests should not be used in women aged over 45 years. This is because FSH fluctuates considerably over short periods of time during the years leading up to menopause and so blood levels are not a helpful addition to what is a clinical diagnosis. If a woman is aged over 45 years and has not had a period for at least 12 months, or has vasomotor symptoms and irregular periods (or just symptoms if she doesn't have a uterus), this is adequate information to diagnose menopause and perimenopause respectively. In younger women, FSH tests should not be used to diagnose menopause in those taking combined oestrogen and progestogen contraception or high-dose progestogen because these affect FSH measurements.

Carrying out this test in this group of women does not improve menopause management and so this is an area of care where considerable savings could be made through disinvestment.

Raising Awareness of the Need to Change Practice

There may be staff in primary care services who do not know that FSH tests should not be carried out in women aged over 45 years.

To raise awareness, clinical commissioning groups, practice managers and lead general practitioners (GPs) could:

- Use newsletters, bulletins and education events to help ensure that GPs and other practice staff (in particular practice nurses) are aware of this change in practice and that they understand the evidence underpinning this recommendation.
- Add a prompt to electronic requesting systems which remind primary care staff that this test should not be requested for women aged over 45.
- Refer GPs to National Institute for Health and Care Excellence (NICE) clinical knowledge summary for menopause.
- Use the NICE costing report and template to estimate the local savings that can be made. A sample calculation using this template showed that savings of £16,500 could be made for a population of 100,000.
- Use the baseline assessment tool to establish current practice in requesting tests and carry out clinical audit so this can be monitored and improved.

Also, laboratory staff and managers could:

- Engage with their local GP practices. For example, in National Health Service (NHS) Lothian a GP/laboratory liaison group meets regularly every 2 months and holds an annual update meeting to which all GPs are invited. This continuing professional development (CPD) accredited meeting provides a good opportunity to promote changes in practice.
- Encourage GPs to stop requesting FSH tests for women aged over 45 years by drawing attention to the fact that this test is unlikely to be informative and is not recommended. Lab Tests Online UK and the UK National External Quality Assessment Service (UK NEQAS) are also raising awareness of the new NICE guidance.

The Challenge: Communicating the Long-term Benefits and Risks of Hormone Replacement Therapy

It is important to provide information on the benefits and risks of hormone replacement therapy (HRT) to help women make an informed choice about which treatment to use for menopausal symptoms. Media reports about HRT have not always been accurate, so providing healthcare professionals and women with a robust source of information is vital. Before publication of this guideline there was no consensus about the long-term benefits and risks of HRT. Although the Women's Health Initiative found that HRT prevented osteoporotic fractures and colon cancer, it initially reported that HRT increased the risk of having a cardiovascular event as well as the incidence of breast cancer. However, the association between HRT and cardiovascular disease has since been disputed and the results show that the risk varies in accordance with individual factors. One of the aims of this guideline is to help GPs and other healthcare professionals to be more confident in prescribing HRT and women more confident in taking it. A knowledge gap among some GPs and other healthcare professionals could mean that they are reluctant to prescribe HRT because they overestimate the risks and contraindications, and underestimate the impact of menopausal symptoms on a woman's quality of life.

Improving Knowledge Among Healthcare Professionals

There is a need to improve knowledge about the long-term benefits and risks of HRT. No other treatment has been shown to be as effective as HRT for menopausal symptoms, though the balance of risks and benefits varies among women. Healthcare professionals need to be in a position to be able to support women to make an informed decision about individual benefits and risks of HRT.

NICE is working with the Royal College of Obstetricians and Gynaecologists (RCOG) to ensure that management of menopause, including the benefits and risks of HRT, is covered within the core curriculum. This includes supporting the update and promotion of the advanced training specialist module on menopause and the subspecialty training in reproductive medicine. They are also working with the Faculty of Sexual & Reproductive Healthcare (FSRH) to highlight the menopause special skills theory course and the basic and advanced special skills module.

To improve knowledge, clinical commissioning group prescribing leads could:

- Help to develop formularies of good HRT prescribing for GPs. This could be done with input from GPs with a specialist interest in menopause and interested consultant gynaecologists.
- Use briefings and newsletters to help disseminate prescribing knowledge on HRT.

Also, GPs could:

- Set up local meetings or teaching sessions (particularly those GPs with a specialist interest) to target interested GPs in each practice who can then take the information back to their partners.
- Use the recommendations in Section 1.5 of the original guideline document and the HRT section of NICE's clinical knowledge summary to ensure that they are informed of the actual long-term benefits and risks of HRT for each individual and are not basing decisions on perceived knowledge.
- Use materials such as NICE's information for the public, NHS choices and the Women's Health Concern leaflet to help support women to make informed decisions when advising them about HRT.
- Link with the menopause specialist in their area for advice. This could be by telephone or email about specific cases and/or through training delivered by the menopause specialist.
- Complete the basic or advanced FSRH special skills course. Practice nurses may also complete this training.

The Challenge: Providing Enough Specialist Services

The number of women aged over 45 years in the UK has been steadily increasing and will continue to rise. The associated increase in the number of women going through menopause is expected to result in more new referrals to secondary care of both women needing short-term symptom control and those with associated long-term health issues. There is currently a lack of specialist services and their availability varies nationally. Throughout this guideline there are recommendations to refer certain women to a healthcare professional with expertise in menopause. Currently, there may not be enough services nationally to refer these women to.

Reviewing and Redesigning Local Service Provision

In order to address variation and potential gaps in service provision, local health services may need to review, map and redesign local service provision.

To do this, commissioners and clinical commissioning groups could:

- Use Menopause UK's national menopause map as a starting point. This highlights variations in practice and the lack of overall provision.
- Clarify current referral routes and communicate them if they are effective.
- Identify lead clinicians to drive a change in service provision if a gap is identified. Ideally all clinical commissioning groups should have a GP with a specialist interest or a community gynaecologist who could do this.
- Establish whether current referrals are appropriate. These may be to secondary care (hospitals), community services or a GP with a specialist interest and will vary according to local facilities. Ideally, services should be provided by a dedicated menopause clinic.
- Confirm that care is provided by a healthcare professional with expertise in menopause (for example, women with breast cancer should have access to a specialist menopause clinic or professional but often receive treatment for menopause from their oncologist who may not have the appropriate training).
- Consider the feasibility of providing dedicated menopause support by setting up clinics within current gynaecology services.
- Menopause clinics may be multispecialist and so jointly led by a nurse consultant and a consultant ensuring that when a member of staff is

unavailable the clinic may still run.
- Establish regional menopause clinics if services are unable to have their own.
- Use the learning from examples of practice where successful services have been set up to help. For example, a primary care service in Essex manages specialist clinic waiting lists through an established agreement whereby a GP with specialist interest accepts emails or written requests from all GPs within a clinical commissioning group. These requests are answered once a week. A specialist service in London has set up a helpline that receives calls outside of clinic times and can allow women to be given support and advice without the need for a clinic appointment.

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Menopause: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Nov 12. 29 p. (NICE guideline; no. 23).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Nov 12

Guideline Developer(s)

National Guideline Alliance - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Collaborating Centre for Women's and Children's Health (NCC-WCH) was commissioned by the National Institute for Health and Care Excellence (NICE) to undertake the work on this guideline.

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

Guideline Development Group Members: Terry Aspray, Consultant Physician, Musculoskeletal Unit, Freeman Hospital; Claire Bowring, Lay member; Melanie Davies, Consultant Obstetrician and Gynaecologist, University College London Hospitals (until November 2014); Deborah Holloway, Nurse Consultant Gynaecology, Guys and St Thomas's NHS Foundation Trust; Sally Hope, GP, Oxford, Oxfordshire; Deborah Keatley, Lay member; Mary Ann Lumsden (*Chair*), Professor of Medical Education and Gynaecology (Clinical Lead for Reproductive and Maternal Medicine), University of Glasgow, and Honorary Consultant Gynaecologist, Glasgow Royal Infirmary; Sara Moger, Lay member; Prunella Neale, Practice Nurse, Herschel Medical Centre, Slough; Nicholas Panay, Consultant Gynaecologist, Specialist in Reproductive Medicine, Queen Charlotte's and Chelsea & Chelsea and Westminster Hospitals, London; Anthony Parsons, Consultant Community Gynaecologist, Coventry and Warwichshire Partnership Trust; Imogen Shaw, GP, Finchingfield, Essex; Christine West, Consultant Gynaecologist, Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh (from Jan 2015)

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Financial Disclosures/Conflicts of Interest

See Appendix C in the full guideline appendices (see the "Availability of Companion Documents" field) for all interests declared between the start of development and submission on 23 March 2015.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site.

Availability of Companion Documents

The following are available:

- Menopause: diagnosis and management. Full guideline. Methods, evidence and recommendations. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12. 283 p. (NICE guideline; no. 23). Available from the National Institute for Health and Care Excellence (NICE) Web site.
- Menopause: diagnosis and management. Appendices. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12.

(NICE guideline; no. 23). Available from the NICE Web site .

- Menopause: diagnosis and management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12. (NICE guideline; no. 23). Available from the NICE Web site .
- Menopause: diagnosis and management. Costing report. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12. 15 p. (NICE guideline; no. 23). Available from the NICE Web site .
- Menopause: diagnosis and management. Costing template. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12. (NICE guideline; no. 23). Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .

Patient Resources

The following is available:

- Menopause: diagnosis and management. Information for the public. London (UK): National Institute for Health and Care Excellence; 2015 Nov 12. 13 p. (NICE guideline; no. 23). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in eBook and ePub formats from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on February 1, 2016. This summary was updated by ECRI Institute on November 17, 2016 following the U.S. Food and Drug Administration advisory on Testosterone and Other Anabolic Androgenic Steroids (AAS).

The National Institute for Health and Care Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Diagnostics guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE diagnostics guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk .

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